UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,679	03/11/2005	Thomas Felzmann	4518-0101PUS1	7223

2292 7590 08/09/2007

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
XIE, XIAOZHEN	

ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
08/09/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/527,679	FELZMANN, THOMAS	
	Examiner	Art Unit	
	Xiaozhen Xie	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *10-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,17 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's amendment of the claims received on 25 May 2007 has been entered.

Election/Restrictions

Applicant argues the finality of the Restriction Requirement. Applicant argues that the following statement in the previous office action amounts to a factual mischaracterization of Ebner's teachings: "Even through Ebner et al. do not express co-stimulation with LPS and IFN-γ, IFN-γ is present in the circulation system since PBLs (both resting and active) secret IFN-γ (see Fig. 9)". Applicant argues that Figure 9 of the Ebner patent teaches dose-response experiments which show that sAIM II stimulates human PBL cells to secret IFN-γ in cell culture. Applicant argues that it is well known that, under physiological conditions, IFN-γ is not present in the circulatory system in amounts sufficient to trigger the release of IL-12 as instantly claimed.

Applicant's argument has been fully considered but has not been found to be persuasive.

The original claim 1 recites "*Use of active dendritic cells (DCs) releasing interleukin 12 (IL-12) which are loaded with an antigen against a specific tumor and, due to the treatment with lipopolysaccharide (LPS) and interderon-gamma (IFN-γ), release IL-12, for the preparation of a medicament for treating a patient having said specific tumor*".

First, the claim provides for the use of DCs, however, the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. Second, the claim is unclear for the recitation "due to treatment with LPS and IFN-γ, release IL-12", because it does not contain technical characterization, and cannot be interpreted as a method step. As indicated in the Restriction Requirement (6 September 2006), the claim is interpreted as "a method for the preparation of a medicament for treating a tumor using active DCs that release IL-12". Ebner et al. teach tumor or non-tumor bearing mice were pre-loaded with tumor-specific antigen, and administered with AIM II proteins (the tumor antigen administered into the mice would have be exposed and loaded into DCs (column 25, lines 44-48). Ebner et al. teach that AIM II stimulates DCs to release IL-12, and that LPS, which is used as a positive control, has similar effect, i.e., stimulates DCs to release IL-12 (column 57, lines 56-67). Ebner et al. teach that LPS increases the AIM II expression (act as an agonist) (column 46, lines 30-32). Ebner et al. further teach employing AIM II polypeptide or an agonist thereof (an agonist is a compound which increases the natural biological functions of AIM II or which functions in a manner similar to AIM II (column 22, lines 37-41)) to treat neoplasia (column 25, lines 22-27; column 3, lines 57-62). Further, IFN-γ is present in the circulation system in activated PBL in the presence or absence of AIM II (Fig. 9). Applicant argues that under physiological conditions, IFN-γ is not present in the circulatory system in amounts sufficient to trigger the release of IL-12 as instantly claimed, however, the claim does not define the "amounts" for IFN-γ, all that required is "releasing IL-12", which has been shown in the Ebner patent.

Thus the technical feature of Group I lacks novelty or inventive step and does not make a contribution over the prior art. The requirement is still deemed proper and is therefore made FINAL.

Claims 17 and 18 have been added. Claims 1-18 are pending. Claims 10-16 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. Claims 1-9, 17 and 18 are under examination.

Claim Objections/Rejections Withdrawn

The rejections of claims 1 and 4 under 35 U.S.C. 112, second paragraph, as being indefinite, are withdrawn in response to Applicant's amendment of the claims.

The objection to claim 1 for a typographical error is withdrawn in response to Applicant's amendment of the claim.

Claim Rejections Maintained

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The amended claims 1, 3-5, 9, and new claims 17, 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Felzmann et al. (Cancer Letters, 2001, July 26, Vol. 168:145-154) ("Felzmann (2001)") for reasons set forth in the previous office action.

Applicant argues that the Felzmann (2001) reference teaches pulsing DCs with an antigen mixture obtained from LCL cultures transformed with Epstein Bar virus

(EBV). Applicant argues that the Felzmann (2001) reference does not teach loading DCs with tumor specific antigens, and does not contain teachings regarding advanced tumors as presently claimed.

Applicants' argument has been fully considered but has not been found to be persuasive.

Felzmann (2001) teaches a method of making mature, antigen-specific DCs *in vitro*, which comprises the steps of: a) collecting mononuclear cells from peripheral blood, adding IL-4 and GM-CSF into the culture and incubating for 7 days to generate an immature DC culture; b) challenging immature DCs with a target cell lysate, e.g., an EBV-transformed LCL cell lysate (pp. 148, right column, section 2.4.); c) exposing the immature DCs to LPS and IFNγ to generate mature DCs (pp. 147, right column, section 2.3.). Felzmann (2001) teach that it might be feasible to use matured DCs for the *in vitro* expansion of antigen-specific T lymphocytes using soluble target cell lysates prepared from any type of tumor (including advanced malignancy) (note that the tumor cell lysates contain tumor-specific antigens), and such DCs could be applied directly as a tumor vaccine (pp. 153, let column, last paragraph in Discussion) and could be used to induce anti-tumor immunity (see Abstract). Therefore, Felzmann (2001) anticipates the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 2 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Felzmann (2001), in view of Asavaroengchai et al. (PNAS, 2002, Jan. 22, Vol. 99:931-936).

Applicant argues that since Felzmann (2001) fails to teach the claimed element of loading DCs with tumor specific antigens, and neither the other prior art reference, nor the combination of the prior art of record rescues this deficiency, the obviousness rejection is improper.

Applicants' argument has been fully considered but has not been found to be persuasive.

As set forth above, Felzmann (2001) teaches each element in the amended claims 1, 3-5 and 9. Felzmann (2001), however, does not teach that the treatment is performed after bone marrow transplantation (BMT). Asavaroengchai teaches that in a therapeutic setting tumor antigen-pulsed DCs can have an impact on residual tumor that remains following BMT (pp. 931, see Abstract and Introduction). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Felzmann (2001), with those of Asavaroengchai, to perform the treatment after bone marrow transplantation.

Claims 6-8 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Felzmann (2001), in view of Rieser (Urol. Int., 1999, Vol. 63(3):151-159), and further in view of Felzmann et al. (Cancer Letters, 2000, Vol. 161:241-250) ("Felzmann (2000)").

Applicant argues that since Felzmann (2001) fails to teach the claimed element of loading DCs with tumor specific antigens, and neither of the other prior art references, nor the combination of the prior art of record rescues this deficiency, the obviousness rejection is improper.

Applicants' argument has been fully considered but has not been found to be persuasive.

As set forth above, Felzmann (2001) teaches each element in the amended claims 1, 3-5 and 9. Felzmann (2001), however, does not teach that the DCs are additionally charged with a tracer antigen that is keyhole limpet hemocyanine (KLH), or additionally charged with an adjuvant tetanus toxoid. Rieser teaches using KLH as a tracer molecule for the determination of the magnitude, kinetics, and T-helper type-1 bias of the cellular and humoral immune response induced by DCs-based immunization (pp. 151, see Abstract). Felzmann (2000) teaches Xenogenization by tetanus toxoid (TT) loading into human tumor cells for anti-tumor immune therapy (pp. 241, Abstract). Felzmann (2000) teaches that unresponsiveness to tumor associated antigens (TAAs) could be overcome when a mixture of TAAs was used together with class II restricted peptides from TT for cell pulsing in vitro (pp. 241, Introduction, 1st paragraph). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Felzmann (2001), with those of Rieser and Felzmann (2000) to additionally load DCs with a tracer antigen KLH and an adjuvant tetanus toxoid.

Conclusion

NO CLAIM IS ALLOWED.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph.D.
July 26, 2007

Eileen B. O'Hara

EILEEN B. O'HARA
PRIMARY EXAMINER